

REMARKS/ARGUMENTS

The new claims correspond to claims filed on November 7, 2006, and subject-matter disclosed in the application as filed. See, e.g., Figs. 2 and 3 where it is evident that the medical product disclosed in this application contains a single dose of tiotropium or a single combined dose tiotropium and at least one additional active pharmaceutical ingredient. No new matter has been added.

The applicant respectfully disagrees with the Examiner that the expression “gradual aerosolization” is vague or indefinite. In addition to the fact that this term is both self explanatory and recognized and understood by those of ordinary skill in the art, the present application includes a reference to published U.S. patent application no. 2003/0192539 A, which in detail discloses an Air-razor device and method implementable in a dry powder inhaler for providing a gradual aerosolization of a dose in a dry powder inhaler. Furthermore, a regular technical dictionary, such as Merriam-Webster’s Collegiate Dictionary, provides a clear meaning to the expression in terms of that the aerosolization proceeds in steps or degrees and developed by fine often imperceptible degrees. Thus, the skilled person realizes that gradual aerosolization means that the single dose or combined dose of the medical product of the present invention is aerosolized during a substantive time interval of the total inhalation and dose delivery time. The gradual aerosolization means that not the whole single dose of the medical product is exposed to an aerosolizing air-stream simultaneously but in clear contrast different portions of the dose will be exposed to the air-stream over the time of the gradual aerosolization. This should be compared to the traditional aerosolization techniques, where the complete dose is exposed to an aerosolizing air-stream, which results in an immediate and not any gradual aerosolization. The rejection should be withdrawn.

The rejection over Davies is traversed. Davies discloses an inhalation device that uses a medicament pack that comprises two sheets peelably secured to one another (paragraph

[0004], [0041]). These two sheets define a large number of medicament containers spaced along the length of the sheets (paragraphs [0003], [0005]). These containers are formed recesses in a roll of the flexible, elongated strip/sheet, denoted base sheet (paragraph [0049]). The recesses are filled with powder and sealed with a common peel-off tape, denoted lid sheet (paragraph [0049]). In connection with inhalation, the two sheets are peeled apart a sufficient portion to expose the contents of a dose pocket, which is being brought into alignment with a slot that is in connection with a nozzle (paragraph [0050]).

The blister pack of Davies is designed to provide an immediate aerosolization of the dose as the whole dose is exposed simultaneously to an inhaled air-stream (see Figs. 4a and 4b). The blister pack of Davies is further designed to contain a large number of doses and blisters, which is consistently stressed in the application and illustrated by the drawings.

Accordingly, Davies does not anticipate, or even suggest, what Applicant is claiming. The rejection should be withdrawn.

The rejection over Pasbrig is traversed. Pasbrig discloses a blister pack comprising multiple (60 to 100) blisters formed in a base sheet (paragraphs [0009], [0010], [0081]). A lid sheet is hermetically sealable to the base sheet except in the region of the blisters and in the leading ends of the sheets (paragraphs [0011], [0019]). The lid sheet can then be mechanically peeled from the base sheet to allow access to medicament powder inside a blister (paragraphs [0011], [0080]).

Different types of medicaments can be used, including tiotropium (paragraphs [0105], [0118]). The drug particles have a diameter of less than 10 μm , typically less than 6 μm (paragraph [0132]). Excipients and carriers may be included (paragraph [0132]).

As the two types of medical products disclosed by Pasbrig, like Davies, are based on the same multi-dose, peelable principles, the patentability of the amended claims is not affected by either of these two documents.

Due to the extremely moisture-sensitiveness of tiotropium, this medicament is not well-suited for usage in connection with multi-dose medical products. The reason for this is that, as has been described in previous responses, such multi-dose products can per se not guarantee that small amounts of water penetrate into at least some of the vast amount (60 to 100) different doses of the products, once arranged in an inhaler device.

The provided Annex B (Borgström et al. "An In Vivo and In Vitro Comparison of Two Powder Inhalers following Storage at Hot/Humid Conditions" Journal of Aerosol Medicine, 18:304-310, 2005) proves that the peelable container solution sold under the trade name DISKUSTM has major moisture problems and it is not tight enough to prevent ingress of moisture.

The provided Annex D (Borgström et al, "Idealhalers or realhalers? A comparison of Diskus and Turbohaler", International Journal of Clinical Practice, 59:1488-1495, 2005) discloses that DISKUSTM product is also marred by low fine particle doses.

The provided Annex A is a picture illustrating the ADVAIRTM product, which is the U.S. correspondence to DISKUSTM but enclosed in a secondary outer protective pouch due to the moisture problems of the peelable container.

Figs. 13 to 16 in Davies are schematic drawings of the product. Thus, by comparing Figs. 13 to 16 in Davies, Annex A and the schematic drawings of provided Annex C (see pages 54 to 58), it is evident to the person skilled in the art that the ADVAIRTM and DISKUSTM products correspond to one of the embodiments of Davies.

These moisture problems are nothing that is unique for the DISKUSTM or ADVAIRTM products but is an inherent limitation of all such peelable, multi-dose medical products. As a consequence, there is today as far as is known not a single product on the market that contains an inhalable medicament that is as water-sensitive as tiotropium enclosed in a peelable, multi-dose package.

Thus, the person skilled in the art is well aware of these water leakage problems of peelable, multi-dose package. Therefore, he/she would when starting from the solutions presented by Davies or Pasbrig search for known solutions to combat moisture penetration problems. For example, it is known to include desiccants together with inhalable medical products. As a consequence, the skilled person would then include such a desiccant in the tiotropium dose in the peelable, multi-dose blister pack of Davies or Pasbrig. The skilled person would therefore not, when starting from the known prior art Davies or Pasbrig, arrive at something falling within the scope of the present claims, as the art directs the skilled person in a totally different direction than was taken by the present inventors.

Such a modification of Davies or Pasbrig has several disadvantages and problems that the present invention does not exhibit. Firstly, a multi-dose, peelable blister pack will have moisture-leakage problems during use causing some of the vast amount of blisters in the blister pack to contain undesired high moisture content levels. These high moisture levels in turn caused powder aggregation and tiotropium instability, which means that correct amounts of tiotropium powder will not consistently be administered at correct lung areas during inhalation of the different blisters in the blister pack.

As the blister packs of Davies and Pasbrig are not adapted for gradual aerosolization, they have problems in providing adequate particle de-aggregation during inhalation, which further lowers the fine particle fraction of the delivered dose.

The inclusion of desiccants can have negative effects by causing irritation in the airways and mouth of the inhaling user. Even though such desiccants generally have larger particle sizes, the particle sizes are distributed around an average size. As a consequence, smaller desiccant particles may indeed reach at least the upper airways but can actually penetrate deeper into the lungs, where they may cause irritation and even local inflammation.

The present invention solves all these problems.

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As shown by the above analysis, no reference alone or in combination with any other reference(s) renders the present claims unpatentable. There is no disclosure of the claimed subject matter, nor is the claimed subject matter rendered obvious. The rejections should be withdrawn.

Finally, the Examiner has made several provisional double patenting rejections. It is submitted that the claims in this case can be passed to Issue in order to first form a firm basis for comparison, after which actual double patenting rejections may be made in the co-pending applications if appropriate during prosecution.

Respectfully submitted,

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